

REMARKS

Claims 27, 28, and 30-32 are pending. No new matter has been added by way of the present amendments. For instance, the claims have been amended to more clearly define the current invention. These amendments are non-narrowing in nature. The language in claim 27 can find support in the present specification at paragraph [0024] on page 9 and paragraph [0041] at page 13 of the present specification. The language from claim 29 has also been added to claim 27. The language in claim 28 is supported by paragraph [0025], the language in claim 30 is supported by paragraph [0053] and the language in claim 31 is supported by paragraphs [0024]-[0025]. New claim 32 is supported by paragraphs [0024], [0089] and [0091]. Lastly, the specification has been amended to correct minor typographical and grammatical errors. A Sequence Listing has also been added. Accordingly, no new matter has been added.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Objection to the Specification

The Examiner has objected to the specification for the reasons recited at pages 2-3 of the outstanding Office Action. Applicants respectfully traverse.

First, the Examiner points out that certain SEQ ID NOs are referenced in the specification without having a corresponding paper and disk version. Applicants traverse and submit that enclosed herewith in full compliance with 37 C.F.R. §§1.821-1.825 is a Sequence Listing to be inserted into the specification as indicated above. The Sequence Listing in no way introduces new matter into the specification. Also submitted herewith in full compliance with 37 C.F.R. §§1.821-1.825 is a disk copy of the Substitute Sequence Listing. The disk copy of the Sequence Listing, file "2003-06-10 3759-0122P.ST25", is identical to the paper copy, except that it lacks formatting.

Second, the Examiner objects to the Abstract of the Disclosure. Applicants traverse and submit that a new Abstract of the Disclosure has been submitted herewith. Accordingly, this objection is moot.

Issues under 35 USC § 112, first paragraph

The Examiner has rejected claims 29 and 30 under 35 USC § 112, first paragraph for the reasons recited at pages 3-4 of the outstanding Office Action. Applicants respectfully traverse.

The Examiner asserts that the method steps of claims 29 and 30 are not supported by the present specification. Applicants disagree with the Examiner. The subject matter of claim 29, now added to claim 27 for clarity, is supported by the present

specification at page 12, paragraph [0037]. Contrary to the Examiner's assertion, the present claims are fully supported by this paragraph, which discloses dissection of a surface loop in a protein to create N- and C-termini. The claims have been amended to more clearly reflect this language. Regarding claim 30, Applicants direct the Examiner's attention to paragraph [0053] at page 16 of the present specification. Accordingly, the language of claims 29 and 30 are fully supported by the present specification. Reconsideration and withdrawal of this rejection are requested.

The Examiner also asserts that there is inadequate written description for the "first" and "second" fusion proteins. Applicants respectfully disagree with the Examiner and traverse this rejection.

The claimed first and second fusion proteins find support in several areas of the present specification, for instance, refer to paragraphs [0002], [0024], [0029], which discuss the first and second fusion proteins. Also refer to paragraph [0041] that includes a definition of "fusion" protein as it relates to the present invention. The Examiner is also referred to originally filed claim 27. Materials and Methods for making such fusion proteins are described in the paragraphs at pages 26-29 of the present specification. Accordingly, Applicants submit that at the time of filing, those having skill in the art would have understood

that Applicants were in possession of the fusion proteins as claimed.

The Examiner also questions how two separate fusion proteins are fused to the two GFP fragments. First, Applicants submit that the proteins to be fused to the GFP fragments are not necessarily fusion proteins themselves, but are, as claimed, a known polypeptide and a test polypeptide. Second, independent claim 27 is not limited to a specific orientation of such fusion (N-, or C-terminal fusion). However, Applicants point out that the claims are limited by the word "linked" meaning that, for instance, the known polypeptide linked to the GFP fragment are not fused in the mid-part of the GFP. Regardless, fusion proteins are well understood in the art.

The Examiner also asserts that the specification does not describe the kind or size of the myriad of known proteins. Applicants submit that the kind, or size of the known proteins is irrelevant. Applicants submit that any protein attached to GFP would behave in the cell as the untagged counterpart. Thus, there is no evidence that a limitation to what kind of proteins can be fused GFP is required.

Also, the Examiner asserts that there is only one discussion of reassembly. Applicants assume that the Examiner is referring to paragraph [0096] at page 29 of the present

specification. Regardless, Applicants are not required to test every possible reassembly.

Absent evidence from the Examiner to the contrary, Applicants submit that the present claims are fully supported by the present specification. Accordingly, the rejections under 35 USC § 112, first paragraph, written description are moot. Reconsideration and withdrawal thereof are requested.

Issues under 35 USC § 112, second paragraph

The Examiner has rejected claims 27-31 under 35 USC § 112, second paragraph for the reasons recited at pages 4-6 of the Office Action. Applicants respectfully traverse these rejections.

First, the Examiner asserts that claim 27 is missing an essential step. Applicants submit that claim 27 has been amended to more clearly reflect the separate steps of the present invention.

Second, the Examiner asserts that claim 28 does not further limit claim 27 since the base claim does not recite a nucleic acid. Applicants disagree with the Examiner. Claim 27 simply requires providing a first and a second fusion protein. Claim 28 requires that these fusion proteins be encoded by a nucleic acid that is transfected or transformed into a host cell and expressed. Thus, claim 28 is narrower in scope than claim 27.

Third, the Examiner asserts that the term "dissection" is confusing in claims 29 and 30. Applicants submit that claim 29 has been cancelled and claims 27 and 30 have been amended to clarify this language.

Fourth, the Examiner asserts that the full names for the acronyms NGFP and CGFP should be provided. Applicants have amended the claims to recite the full names of these acronyms.

In summary, Applicants respectfully submit that the present claims define subject matter which is fully definite as required by 35 USC § 112, second paragraph. Reconsideration and withdrawal of these rejections is therefore requested.

Issues under 35 USC § 103(a)

The Examiner has rejected claims 27-31 under 35 USC § 103(a) as being obvious over either Michnick et al., WO 01/00866 (hereinafter referred to as Michnick), or Mayer, US 2002/0037999 (hereinafter referred to as Mayer) in view of either Anderson et al., USP 6,180,343 (hereinafter referred to as Anderson) or Katz et al., Biotechniques (hereinafter referred to as Katz). Applicants respectfully traverse this rejection.

As a preliminary note, Applicants point out that Michnick is not prior art. Michnick (WO01/00866) has a publication date of January 4, 2001, which is after the present application's

priority date of May 12, 2000. Thus, Michnick does not qualify as prior art.

The Examiner asserts that it would have been obvious to one of ordinary skill in the art to substitute the enzymes of either Michnick or Mayer with the GFP of Katz or Anderson. Even if Michnick is included in this rejection, the Examiner has still failed to present a *valid prima facie* case of obviousness.

First, Applicants submit that none of the references cited by the Examiner discusses using a split detectable marker to identify protein interactions between a known protein and a test protein. Thus, the Examiner has failed to establish a *prima facie* case of obviousness.

Second, none of the references cited by the Examiner suggest or disclose that a full length GFP can be split (dissected) at a surface loop and used in the presently claimed method. None of the references discloses such a limitation.

Applicants note that the Examiner cites Anderson as disclosing N- and C-termini of GFP fused to random peptides. However, a distinction exists. While Anderson want to avoid local distortions in the GFP structure since this is feared to destabilize folding intermediates or allow access to GFP's buried tripeptide fluorophore and subsequently decrease or even eliminate GFP's fluorescence (column 16, lines 17-26 of Anderson), the present invention has realized that a total

dissection (expression of two halves of GFP independently) is capable of forming functional GFP when brought close together by proteins with affinity for each other (see the Examples of the present application as filed). This is a limitation of the present claims, which is neither suggested nor disclosed by the cited references, whether taken individually or in combination. Accordingly, no *prima facie* case of obviousness exists.

In view of the above remarks, Applicants respectfully submit that the present claims define subject matter that is patentable over the cited art and fully complies with the requirements of 35 USC § 112, first and second paragraph. Accordingly, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.


Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie (Reg. No. 42,874) at the telephone number of the undersigned below.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of one (1) month to June 13, 2003 in which to file a reply to the Office Action. The required fee of \$110.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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